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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,789	02/12/2002	Todd R. Golub	WIBL-P02-518	8072
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FISH & NEAVE IP GROUP ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			EXAMINER MORAN, MARJORIE A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 11/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/074,789

Applicant(s)

GOLUB ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 7-14, 65, 66 and 71 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-14 and 71 is/are rejected.
- 7) ☒ Claim(s) 6, 65 and 66 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

All rejections and objections not reiterated below are hereby withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 1-14, 65-66, and 71 are pending.

***Election/Restrictions***

The species of AML and ALL were found free of the prior art, therefore the search was expanded to include previously nonelected species recited in claims 65-66. Claims 65 and 66 are hereby rejoined with elected claims 1-14, and 71 and an action on the merits of pending claims 1-14, 65-66 and 71 follows.

***Claim Rejections - 35 USC § 112***

Claim 7 is again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments filed 8/15/05 have been fully considered but they are not persuasive. In response to the argument that the examiner's concern "is based solely on the fact that certain genes in the list are capitalized", it is noted that the rejection set forth in the previous office action did not state anything with regard to capitalization. Relevant portions of the rejection are reiterated below:

"(A)s the list recited is NOT one of genes, it is again unclear what limitation applicant intends and the claim is again indefinite. In response to applicant's arguments, it is noted that "gene expression products" are defined as being proteins,

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peptides or nucleic acid molecules on page 21 of the specification; however, as “informative genes” are not defined to BE proteins, and those skilled in the art generally consider proteins and nucleic acids to be different biochemical molecules, the limitation of “informative genes” to be proteins is confusing...”

It is noted that many of the compounds recited in claim 7 are well-known to be proteins; e.g. cyclin, topoisomerase, catalase. Further, whether capitalized or not, many of the names are those associated with proteins, not genes; e.g. IL-7 receptor, CD33, ATPase. Claim 7 specifically limits “the informative genes” to be selected from the recited list of compounds. However, as the compounds recited in claim 7 are those of proteins, not genes, claim 7 is still indefinite. It is recognized that applicant may have intended to recite genes which encode the recited proteins. Unfortunately, support for such a limitation is not found in the originally filed disclosure, as set forth in a previous office action. It is noted that a gene encoding ATPase, for example, may differ in structure/sequence from one organism to another. Therefore, even if applicant intended genes which encode the recited proteins, it would not be clear which particular gene(s) were intended. For these reasons and those previously set forth, the examiner maintains that claim 7 is indefinite.

### ***Claim Rejections - 35 USC § 103***

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection. Applicant's arguments with regard to the AML and ALL data of BARNHILL are persuasive, therefore the rejection of claim 6 is

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withdrawn. See also the reasons for indicating allowable subject matter, set forth below. However, applicant has not set forth any arguments with regard to generic claims (i.e. those NOT specifically directed to AML/ALL). As ZHENG and EISEN make obvious the limitations of claims directed to generic disease classes and specifically, to cancer, as set forth below, the examiner maintains that ZHENG and EISEN make obvious claims 1-5, 7-14, and 71.

Claims 1-5, 7-14 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over ZHENG et al. IEEE Transactions on Neural Networks, (11/1997) vol. 8 (6), pp. 1386-1396) in view of EISEN et al. (IDS ref AV: PNAS (12/1998) vol. 95, pp. 14863-14868).

ZHENG teaches a method of classifying malignant vs. benign breast tissue using weight adjustments (i.e. a weighted "voting" scheme), summation of votes and use of a prediction threshold (confidence level) to determine a winning class (pp. 1389-1390). ZHENG does not teach use of informative genes nor use of a statistical routine. ZHENG does not specifically teach a clustering routine.

EISEN teaches a method of clustering genes using a Euclidean routine to determine similarity (p. 14863). EISEN teaches that weighting may be used to order his genes (p. 14864), and teaches clustering of genes encoding many of the same proteins listed in instant claim 7 (Figure 2).

It would have been obvious to one of ordinary skill in the art to have combined ZHENG's weighted voting scheme, summation of votes, and confidence level

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threshold/cutoff with EISEN's Euclidean routines to cluster and classify genes involved in cancer, specifically the leukemia of BARNHILL, where the motivation would have been to organize data in manner intuitive for biologists, as taught by EISEN (abstract). One skilled in the art would reasonably have expected success in combining the classification method of ZHENG with the classification of gene expression data of EISEN because both teach similar statistical methods of clustering and classification of biological/array data.

***Allowable Subject Matter***

Claims 6 and 65-66 are each objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: applicant's arguments with regard to BARNHILL's AML and ALL data, set forth in the response filed 8/15/05, are persuasive. The prior art of DECAESTECKER et al. (J. Neuropathology and Exp. Neurology (1995) vol. 54, no. 3, pp. 371-384) teaches use of supervised learning algorithms to classify glioblastomas, but does not teach or suggest doing so using expression levels of informative genes. None of the prior art teaches or fairly suggests methods of classifying medulloblastoma, follicular lymphoma, or diffuse large B cell lymphoma using informative gene expression levels and a weighted voting scheme.

**Conclusion**

Claims 1-5, 7-14 and 71; claims 6 and 65-66 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon,Wed: 7-1:30; Tue,Thur: 7:30-6; Fri 7-3:30 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran  
Primary Examiner  
Art Unit 1631

*Marjorie A. Moran*  
10/31/05